REMARKS

Claims 1-16 and 36-38 presently appear in this case. No claims have been allowed. The official action of April 20, 2004, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a method for activating natural killer cells in a human patient by administering an effective amount of an adenosine A3 receptor agonist (A3RAg). The agonist will activate the NK cells by fully or partially activating the adenosine A3 receptors on the NK cells. This method may be used to treat diseases that are sensitive to activated NK cells, such as the treatment of tumor cells, malignant and infectious diseases, immunoregulation, hematopoiesis and neuroendocrine interactions.

The undersigned was in contact with Examiner Lewis about scheduling an interview in this case on July 15 or 16, 2004. On July 9, the undersigned received a telephone call from Examiner Lewis, who advised the undersigned that in reviewing the case in preparation for the interview, he now agreed with our previous arguments that Williams teaches away from the invention, and that he was considering withdrawal of this rejection. Accordingly, the interview was canceled for the time being. On July 15, 2004, Examiner Lewis again

contacted the undersigned by telephone, stating that while the present art rejection would be withdrawn, he now considered that claim 1 was anticipated by the disclosure of the Jacobson patent 5,773,423. The examiner stated that claim 1 is written broadly enough to read on administering IB-MECA, for example, to any human being for any purpose, and that the result of activation of NK cells will inherently happen when it is being administered for any purpose, such as for one of the purposes specified in columns 25 and 26 of the Jacobson patent. The undersigned inquired whether claim 9 would be subject to such a rejection. After reviewing claim 9, the examiner called back and advised the undersigned that claim 9 would also be considered to be anticipated by Jacobson, in view of the fact that claim 9 reads on treatment of "reproduction", and Jacobson at column 25, line 27, states that one of the indications for administering an A3RAg is "infertility". The courtesies extended in these telephone interviews are gratefully acknowledged.

The present amendment is being filed in order to amend the claims in a manner so as to avoid the new ground of rejection raised in the telephone interview under 35 U.S.C. §102 over Jacobson et al. Claim 1 has now been amended to specify that the A3RAg is administered to a human in need of activation of natural killer (NK) cells. Thus, claim 1 no

longer reads on administering the A3RAg to any person for any purpose, but is now directed only to a method for activating NK cells in a human being of need thereof. In order to avoid the accidental overlap between the indications of Jacobson and those of the present invention, a proviso has been added to claim 1 that the human being in need is other than one in need of treatment for reproductive problems. As treatment relating to "reproduction" is one of the specific indications previously appearing in claim 9, a proviso excluding one of the previously set forth species complies with the written description requirement of 35 U.S.C. §112. As stated at MPEP 2173.05(i):

> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977))("[the] specification, having described the whole, necessarily described the part remaining.").

Claim 9 has further been amended to change the language thereof somewhat, to remove the recitation of specific diseases therein, and insert the recitation of those specific diseases in dependent claim 38. Claim 9, however, does include the same proviso that the disease or disorder is other than one related to reproduction. Thus, claim 9 now more clearly defines the method for treating a disease or disorder in a human individual that may be ameliorated through

activation of NK cells. Accordingly, all of the present claims have now been amended in such a manner so as to avoid anticipation by Jacobson. Reconsideration and withdrawal of this prospective rejection, and allowance of all the claims now present in the case are therefore respectfully urged.

In view of the withdrawal of all of the previous rejections, and the prospective introduction of a new anticipation rejection, it is respectfully requested that the finality of the official action of April 20, 2004, be withdrawn, so that the present amendment can be entered. Whether or not the finality is withdrawn, it is respectfully submitted that the present amendment is in response to a new ground of rejection first raised in a telephone interview on July 15, 2004. The present amendment should be entered under 37 C.F.R. §1.116, as there is good reason why it was not earlier presented. Furthermore, it is believed that the present amendment places the case into condition for allowance. If there is any question about the allowability of claims with the language presented herein, it is respectfully requested that the examiner contact the undersigned by telephone, so that any remaining issues can be worked out, and the present application can proceed to issue.

In the final rejection of April 20, 2004, claims 1-16 were rejected under 35 U.S.C. §103(a) as being unpatentable over Williams and Jacobson. The examiner points out that applicant's arguments filed June 30, 2003, argue that Williams

teaches away from adenosine receptor binding. The examiner states that it would have been obvious to one of ordinary skill in the art to modify the 2-chloroadenosine of Williams to enhance the activation of natural killer cells. This rejection is respectfully traversed.

Applicant's arguments filed June 30, 2003, are hereby repeated and incorporated herein by reference. Williams teaches away from the method of the invention in that he explicitly teaches that 2-CA does not stimulate NK cells through the A3 receptor, nor through any other adenosine receptor. One of ordinary skill in the art would therefore have had no reason to combine Williams with Jacobson, since Jacobson teaches modification of adenosine to moderate A3 selectivity, while Wiliams teaches away from adenosine receptor binding. Accordingly, the method of the present invention would not have been obvious from any combination of Williams and Jacobson.

As indicated above, the examiner advised in telephone interviews that the repeated rejection has been reconsidered and withdrawn. For the record, applicant hereby again requests that this rejection be officially reconsidered and withdrawn.

Claims 36 and 37 have also been rejected under 35 U.S.C. §103(a) as being unpatentable over Williams and Jacobson in combination. The examiner's reasoning is substantially the same as discussed above with respect to the

rejection of claims 1-16. This rejection is respectfully traversed.

The present rejection is not applicable for the same reason as discussed above with respect to the rejection of claims 1-16. Williams teaches away from the present invention in that he discloses that his main compound does not stimulate NK cells through the A3 receptor, nor through any other adenosine receptor. Thus, it would not have been *prima facie* obvious to combine the references for any reason. Reconsideration and withdrawal of this rejection, as indicated by the examiner in the telephone interview, is therefore also respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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July 21, 2004
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